

Remarks/Arguments

The foregoing amendments to the claims are of formal nature, and do not add new matter. Prior to the present amendment, claims 39-44 were pending in this application and were rejected on various grounds. Claim 44 has been canceled without prejudice and claims 39 has been amended. The rejections to the presently pending claims are respectfully traversed.

Sequence compliance

2) Applicants have deleted the sequences on page 2, line 37 and page 14, line 17 of the specification which should overcome this objection.

Oath/Declaration

3) Applicants have enclosed a new combined declaration executed by Wei-Qiang Gao which should overcome this objection.

Specification

5) The specification has been objected to for containing an embedded hyperlink. The foregoing amendment, which deletes all embedded hyperlinks or other forms of browser executable code, is believed to overcome this objection.

6) Applicants submit that Table 1 is a computer program while Tables 2-6 comply with 37 C.F.R. 1.55(c) format.

Claim Rejections – 35 USC § 101

7) Claims 39, 40 and 44 were rejected under 35 U.S.C. §101 allegedly because "the claims failed to include limitations which would distinguish the claimed antibodies from those which occur in nature."

8) Claims 39-44 were also rejected under 35 U.S.C. §101 because the claimed invention was drawn to an invention with no apparent or disclosed specific and substantial credible utility.” The Examiner specifically noted that “the instant specification does not disclose a credible "real world" use for the disclosed nucleic acid or the protein encoded thereby.”

The rejection is respectfully traversed.

Utility – Legal Standard

According to the Utility Examination Guidelines (“Utility Guidelines”), 66 Fed. Reg. 1092 (2001) an invention complies with the utility requirement of 35 U.S.C. § 101, if it has at least one asserted “specific, substantial, and credible utility” or a “well-established utility.”

Under the Utility Guidelines, a utility is “specific” when it is particular to the subject matter claimed. For example, it is generally not enough to state that a nucleic acid is useful as a diagnostic without also identifying the conditions that is to be diagnosed.

The requirement of “substantial utility” defines a “real world” use, and derives from the Supreme Court’s holding in *Brenner v. Manson*, 383 U.S. 519, 534 (1966) stating that “The basic *quid pro quo* contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility.” In explaining the “substantial utility” standard, M.P.E.P. 2107.01 cautions, however, that Office personnel must be careful not to interpret the phrase “immediate benefit to the public” or similar formulations used in certain court decisions to mean that products or services based on the claimed invention must be “currently available” to the public in order to satisfy the utility requirement. “Rather, **any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient**, at least with regard to

defining a "substantial" utility." (M.P.E.P. 2107.01, emphasis added.) Indeed, the Guidelines for Examination of Applications for Compliance With the Utility Requirement, set forth in M.P.E.P. 2107 II (B) (1) gives the following instruction to patent examiners: "If the applicant has asserted that the claimed invention is useful for any particular practical purpose . . . and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility."

Finally, the Utility Guidelines restate the Patent Office's long established position that any asserted utility has to be "credible." "Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record . . . that is probative of the applicant's assertions." (M.P.E.P. 2107 II (B) (1) (ii)) Such standard is presumptively satisfied unless the logic underlying the assertion is seriously flawed, or if the facts upon which the assertion is based are inconsistent with the logic underlying the assertion (Revised Interim Utility Guidelines Training Materials, 1999).

Proper Application of the Legal Standard

Applicants rely on the skin vascular permeability assay (Example 77, page 210, lines 22 onwards) to establish patentable utility for the polypeptide PRO266. These results were first disclosed in international application PCT/US98/19437, filed 17 September, 1998 to which priority is claimed in this application. Accordingly, the present application is entitled to the effective filing date of 17 September, 1998.

The present claim amendments recite antibodies that "specifically" bind to the PRO226 polypeptide and "wherein said antibody is capable of inhibiting an inflammatory response."

Example 77 describes a dye-based proinflammatory cell infiltration assay in which PRO226 induces mononuclear cell, eosinophil and PMN infiltration into the site of injection of this peptide/protein into an animal.

In the proinflammatory cell infiltration assay, purified or conditioned media containing PRO226 was injected intradermally onto the backs of hairless guinea pigs whereas the Evans blue dye was injected intracardially. Blemishes at the injection sites were measured 1 h and 6 h post injection. Animals were sacrificed at 6 h after injection, the skin at each injection site was biopsied, fixed in formalin and evaluated histopathologically for inflammatory cell infiltration into the skin. Such inflammatory cell infiltration assays are routinely used in the art to evaluate proinflammatory properties of novel compounds (see Rampart et al; enclosed in IDS). For example, in Rampart et al., IL-8 (Interleukin 8) was identified using a neutrophil accumulation assay in rabbit skin (see Methods, page 22) and the findings were correlated with albumin flux and neutrophil dependent edema in skin.

During proinflammatory conditions, several mechanisms act synergistically to mediate an increase in neutrophil accumulation, plasma extravasation, etc. Such events occur for example, during the acute phase of an inflammatory response to a microbial stimulus or during pathologic conditions like graft rejection, edema, psoriasis, arthritis, tissue injury etc. For example, the enclosed reference, Rampart et al. indicates that endogenous IL-8 could be involved in the acute phase of an inflammatory response to a microbial stimulus and further disclosed suggestive data to support its involvement in psoriatic patients (see page 24, column 1, last paragraph). Subsequent knowledge in the art has shown many important biological roles for IL-8; for example: IL-8 has been shown to be part of the cytokine cascade in the synovium of patients suffering from rheumatoid arthritis; further, IL-8 is associated with other inflammatory diseases like asthma, leprosy, psoriasis, inflammatory bowel disease, atherosclerosis, cystic fibrosis,

and in various respiratory syndromes. IL-8 has been shown to induce tumor growth, an effect attributed to its angiogenic activity while administration of anti-IL-8 to SCID mice bearing xenografts of IL-8-expressing human lung cancer has been shown to have beneficial effects. Similarly, a variety of real-life utilities are envisioned for PRO226 based on the proinflammatory cell infiltration assay results.

Accordingly, antibodies raised against PRO226 can be exploited for their anti-inflammatory properties.

As set forth in M.P.E.P, 2107 II (B) (1), if the applicant has asserted that the claimed invention is useful for any particular practical purpose, and the assertion would be considered credible by a person of ordinary skill in the art, a rejection based on lack of utility should not be imposed. Indeed, the logic underlying Applicants' assertion that PRO266 may be useful in boosting an immune response is not inconsistent with the general knowledge in the art, and would be considered credible by a person skilled in the art. It is always possible that an invention might fail on its way of development to a commercial product. For example, despite recent advances in rational drug design, a large percentage of drug candidates fails, and never makes it into a drug product. However, the USPTO is not the FDA, the law does not require that a product (drug or diagnostic) be currently available to the public in order to satisfy the utility requirement.

Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

Claims Rejections - 35 USC § 112, First Paragraph

8. Claims 39-51 were rejected under 35 U.S.C. §112, first paragraph, since allegedly, the claimed invention is not supported by either a clear asserted utility or a well established utility for the reasons set forth above, thus one skilled in the art would not know how to use the claimed invention.

Present claim amendments recite antibodies that "specifically" bind to the PRO226 polypeptide and "are capable of inhibiting an inflammatory response" which is a specific and substantial asserted utility. Based on the information disclosed in the specification and that available in the art, one skilled in the art knew how to practice the claimed invention, at the effective priority date of this application, without undue experimentation. As the M.P.E.P. states, "The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *In re Certain Limited-charge cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), *aff. sub nom.*, *Massachusetts Institute of Technology v A.B. Fortia*, 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985) M.P.E.P. 2164.01.

Hence, withdrawal of this rejection is requested.

Claims Rejections -35 USC § 112, Second Paragraph

Claim 44 was rejected under 35 U.S.C. §112, second paragraph, as alleged's indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Specifically, claim 44 is vague and indefinite for recitation of "specifically binds to" without reciting the metes and bounds of the recitation.

Claim 44 has been canceled without prejudice or disclaimer; hence this rejection is moot. Claim 39 has been amended to recite: antibodies that "specifically" bind to the PRO226 polypeptide and "wherein said antibody is capable of inhibiting an inflammatory response or is useful as a diagnostic agent." One of skill in the art would understand that by "specifically" is meant and antibody that binds an epitope unique to the PRO226 polypeptide and hence these antibodies are distinct. In addition, the claim also recites a

functional characteristic of inhibiting inflammatory response or being useful as a diagnostic agent. Thus, Claim 39 is definite and this rejection should be withdrawn.

Claim Rejections - 35 USC § 103

Applicants acknowledge the Examiner's quote regarding joint inventors and submit that the subject matter of the various claims were commonly owned at the time the invention was made.

12. Claim 39 was rejected under 35 U.S.C. 103(a) as being unpatentable over Mochly-Rosen et al. (U.S.P.N. 5,519,003).

The Examiner alleges that the '003 patent discloses an amino acid sequence which comprises an epitope of 6 contiguous amino acids which are identical an epitope of SEQ ID NO: 91.

The '003 patent discloses a protein with a 7 amino acid stretch identical to PRO266. It also discloses antibodies to said protein for detecting this protein in a protein overlay assay. Patent '003 does not disclose or anticipate polypeptides associated with an inflammatory response nor preparation of antibodies capable of inhibiting an inflammatory response.

On the other hand, the current invention claims antibodies that specifically bind to the polypeptide shown in Figure 46 (SEQ ID NO:127) or PRO266, wherein said antibody is capable of inhibiting an inflammatory response.

As the Examiner is aware, to establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when

combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). See M.P.E.P. 2143.03

Applicants submit that the '003 patent does not motivate one of skill in the art to make or use its antibodies for inhibiting an inflammatory response or as diagnostic agents for identifying inflammatory diseases. Additionally, all the present claim limitations are not taught by the '003 patent since the foregoing amendments to claim 39 distinguish the claimed antibodies over the '003 patent antibodies. The combination of the '003 patent with the knowledge in the art, which is applied only to show that antibodies to the 7 amino acid stretch would be known in the art at the effective priority date of the present application, does not make obvious the pending claims. Thus, Applicants respectfully request the reconsideration and withdrawal of the present rejection.


The present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 08-1641 (Attorney

Docket No.: 39780-1618P2C30). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

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